

Attorney Docket No.: **ISPH-0500**
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REMARKS

Claims 1-11 are pending in the instant Office Action. Claims 1-11 have been rejected. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. 102(b)

Claims 1, 3, 8 and 9 have been rejected under 35 U.S.C. 102(b) as being anticipated by Temsamani et al. (1993). The Examiner suggests that this paper teaches a method for detecting or quantitating an oligonucleotide in a bodily fluid or extract comprising contacting said fluid or extract with a probe complementary to said oligonucleotide wherein said probe includes a detectable moiety and placing said fluid or extract in contact with a solid support (nylon membrane) to which a binding partner of said binding moiety is attached and contacting said fluid or extract with a nuclease and detecting a label associated with said marker wherein the presence of said label indicates the presence of said oligonucleotide bound to said solid support. Further, the Examiner suggests that this paper teaches that the oligonucleotide can comprise at least one phosphorothioate linkage and that digoxigenin can be used as a labeling compound and well as the use of chemiluminescence. Applicants respectfully disagree with the

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Examiner's analysis and conclusions regarding the teaching of this paper.

Temsamani et al. (1993) teaches a method for quantitation and detection of phosphorothioate modified oligonucleotides. The first step in this method is explicitly stated in the Abstract and shown in Figure 3 as being immobilization of the oligonucleotide to a solid support, in this case a nylon membrane, BEFORE the oligonucleotide is contacted with any type of binding probe. In the present method, the claims state and the specification teaches that the binding moiety of the probe, NOT the oligonucleotide itself, is what binds directly to the solid support. Therefore, this paper does not teach the instant claims which do not require or suggest that the oligonucleotide itself is first immobilized on a solid support before contact with a binding probe. Accordingly, this paper does not anticipate the instant claims as it teaches a very different first step. Withdrawal of this rejection is respectfully requested.

II. Rejection of Claims Under 35 U.S.C. 103(a)

Claim 2 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Temsamani et al. and further in view of Serres et al. The Examiner suggests that it would have been *prima facie*

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obvious to one of ordinary skill to combine the oligonucleotide detection method of Tamsamani et al. with the method of Serres et al. for detecting oligonucleotides in plasma. Applicants respectfully disagree with the Examiner's conclusions.

As discussed *supra* in Section I, the primary reference of Tamsamani et al. (1993) fails to teach the instant invention as claimed. Therefore, the combination of Serres et al., which teaches detection of oligonucleotides in plasma by another very different method does not render the instant invention obvious. To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as filed. Withdrawal of this rejection is respectfully requested.

Claims 4-7 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Tamsamani et al., and further in view of Lind et al. (1998) and Prosnyak et al. (1994). The Examiner suggests it

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would have been *prima facie* obvious for one of ordinary skill to combine the oligonucleotide method of Temsamani et al. with the Lind et al. method for modification of oligonucleotides with at least one sugar moiety at the 2' position and with the Prosnyak modified base wherein said modified base is 5-methylcytosine. Applicants again respectfully disagree with the Examiner's conclusions.

As discussed *supra* in Section I, the primary reference of Temsamani et al. (1993) fails to teach the instant invention as claimed. Therefore, the combination of two secondary references (Lind et al. and Prosnyak) which teach only methods for modifying oligonucleotides does not render the instant invention obvious. To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as filed. Withdrawal of this rejection is respectfully requested.

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Claims 10 and 11 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Tamsamani et al., and further in view of Lundin et al. (1997). The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill to combine the Tamsamani detection method with the Lundin S1 nuclease to make the claimed invention. Applicants respectfully disagree with the Examiner's conclusions.

As discussed *supra* in Section I, the primary reference of Tamsamani et al. (1993) fails to teach the instant invention as claimed. Therefore, the combination of Lundin et al., which teaches a method for screening large regions of DNA for structural changes, a very different method for a different purpose, does not render the instant invention obvious. To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the cited combination cited fails to teach or suggest the limitations of the claims as filed. Withdrawal of this rejection is respectfully requested.

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III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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